

REMARKS

Claims 1-13 are all the claims pending in the application. Claims 4-5 and 7-12 are withdrawn from consideration.

Claims 1-3, 6 and 13 are rejected under 35 U.S.C. §103(a) as being unpatentable over Muramatsu et al (International Publication No. W099/15202), in view of Ishizuka (Geriatric Medicine, Vol. 41, No. 8, pages 1149-1153; 2003), as evidenced by Ohashi et al (Caretaker Group Federation Monthly, Vol. 8, No. 591, pages 57-60; 1998) and Garvey et al. (U.S. Patent Application Publication No. 2002/0143007A1).

With regard to instant claims 1-3, 6 and 13, the examiner asserts that Muramatsu et al disclose, in the Abstract, remedies for dysuria resulting from prostatic hypertrophy, which contain a highly selective α -adrenergic receptor blocker, e.g., silodosin.

The Examiner recognizes that Muramatsu et al fail to disclose specifically wherein the remedies, or methods, are for the treatment of overactive bladder accompanied with neurogenic disorders, e.g., spinal cord involvement.

However, the Examiner relies on Ishizuka as disclosing, at page 11 of the document, that α receptors are extremely important in the manifestation of overactive conditions. The Examiner relies on Ishizuka as further disclosing an overview of the relation between overactive bladder, which is a new concept having urination urge as its chief symptom and hypertrophy of the prostate gland. According to the Examiner, Ishizuka discloses that α blockers are the main therapeutic agent for hypertrophy of the prostate gland. On page 4, Ishizuka discloses that spinal cord injuries and other nerve impairments are factors which cause overactive bladder.

The Examiner relies on Ohashi et al for evidentiary purposes as disclosing that hyperactive bladder and unstable bladder are illnesses which cause urge incontinence. In the instant excerpt, Ohashi et al further disclose that hyperactive bladder is a sequelae to cerebral hemorrhage, Parkinson's disease and spinal damage.

Additionally, Garvey et al is relied on as disclosing, in reference claims 37, 38 and 51, pages 47 and 48, a method for treating benign prostatic hyperplasia, a neurodegenerative disorder, urge incontinence or overactive bladder in a patient in need thereof comprising administering to the patient a composition comprising KMD 3213 (silodosin).

The Examiner concludes that a skilled artisan would have envisaged the instantly claimed method for the treatment of overactive bladder accompanied with spinal cord involvement, as disclosed by Muramatsu et al, in view of Ishizuka, as evidenced by Ohashi et al Garvey et al. the Examiner further asserts that one of ordinary skill in the art would have been motivated to combine the teachings of the aforementioned references when seeking a method that effectively treats overactive bladder wherein a pharmacotherapy is preferred without the need of a risky and an invasive surgery.

Applicants traverse the rejection and submit that there is no motivation for one of ordinary skill in the art to combine the references as suggested by the Examiner with a reasonable expectation of success in achieving the claimed invention, i.e., a method of treating overactive bladder accompanied with neurogenic disorders. Even if the references could be combined, the claimed invention would have been achieved.

As described in the specification of the present application, Overactive Bladder (OAB) is defined as a disease based on symptoms of urgency, usually with frequency and with or without urge incontinence. OAB is a urinary disorder in filling phase, which develops accompanied with neurogenic disorder, lower urinary tract obstruction or others (see paragraphs [0004] and [0005]). That is, BPH (a disease with lower urinary tract obstruction) is one of the causes to develop OAB, and OAB accompanied with BPH (BPH-OAB) is distinct from OAB accompanied with neurogenic disorder (neurogenic OAB), and these are caused by different conditions. This is also described in Ishizuka (from p. 1149, right column, the last line to p. 1150, left column, line 5). None references cited by the Examiner discloses any teaching of combining BPH-OAB and neurogenic OAB.

Muramatsu discloses remedies for voiding dysfunction resulting from prostatic hypertrophy (BPH), which contains a highly selective $\alpha 1$ -adrenergic receptor blocker, silodosin, but does not disclose methods for the treatment of OAB or neurogenic OAB at all. Ishizuka also discloses some relationship between BPH-OAB and $\alpha 1$ -adrenergic receptor, but does not disclose anything about neurogenic OAB. As the Examiner points out, Ishizuka discloses that $\alpha 1$ -adrenergic receptors are extremely important in the manifestation of overactive conditions, but it is clear that this is mentioned based on the experiments using lower urinary tract obstruction-induced rat OAB model.

Therefore, while both references (Muramatsu and Ishizuka) only describe BPH or BPH-OAB, they do not give any motivation for skilled artisan to use an $\alpha 1$ -adrenergic receptor blocker, silodosin, for the treatment of neurogenic OAB. As mentioned above, BPH-OAB and neurogenic OAB are developed by different causes, and thus, it is unobvious to predict that silodosin is useful for the treatment of neurogenic OAB even though there might have been teachings that silodosin is useful for the treatment of BPH or BPH-OAB.

Applicants submit that neither Ohashi nor Garvey provide any evidence of the obviousness of the present invention over Muramatsu in view of Ishizuka. Ohashi actually discloses that hyperactive bladder and unstable bladder are illnesses which cause urge incontinence, and hyperactive bladder is a sequelae to cerebral hemorrhage, Parkinson's disease and spinal damage. Ohashi discloses a use of $\alpha 1$ -adrenergic receptor blocker only for treatment of voiding dysfunction in elder men or in BPH patients. Thus, Ohashi describes only neurogenic OAB but nothing about any effect of $\alpha 1$ -adrenergic blocker for the treatment of neurogenic OAB.

Garvey only discloses a method of treating or preventing sexual dysfunctions, which contains administering an $\alpha 1$ -adrenergic receptor antagonist in combination with one or more compounds that donate, transfer or release nitric oxide or the like, and just lists BPH, urge incontinence, overactive bladder and so on.

Therefore, even if the cited references were combined (a point Applicants do not concede), the presently claimed invention would not have been achieved since there are no descriptions or suggestions to use silodosin for treating neurogenic OAB.

Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below. The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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